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FERMENTATION, PUTREFACTION AND SUPPURATION

WITH

DEMONSTRATIONS AND EXPERIMENTS

BY

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FERMENTATION, PUTREFACTION, AND SUP- PURATION, WITH DEMONSTRATIONS AND EXPERIMENTS.¹

MR. PRESIDENT : Will you kindly allow me a few introductory remarks on the importance of bacteriology in the study and practice of medicine.

Last summer I was struck by the first sentence² of a paper on Ptomaines, read by Professor Brieger, of Berlin, before the Congress of German Physicians at Wiesbaden, April 14, 1886, viz.: "The different forms of infectious diseases which constitute the bulk of all cases of sickness, are, according to the present standpoint of science, all caused by specific bacteria." This statement surprised me so much the more, as I had had, a few days before, a conversation on bacteriology with a celebrated professor of one of our New York colleges. "Bacteriology," said he, "is of great scientific interest, but in practice what does it signify? *Six diseases!*" This divergence of opinion induced me to seek for some statistics of germ-diseases. Looking up the death reports printed in different medical journals, I found the most extensive records in the *Boston Medical and Surgical Journal*, namely, weekly statements of reported mortality of the principal American cities. In the number for Septem-

¹ Discourse delivered before the New York Academy of Medicine, December 16, 1886.

² Berl. klin. Wochensch., Mai 3, 1886.

ber 2, 1886, I found the following for the week ending August 21st:

New York, with an estimated population of 1,493,039, 736 deaths, of which from

	Per cent.
Infectious diseases.....	33.30
Consumption.....	16.38
Croup and diphtheria.....	4.90
Total.....	54.58

In the other cities the returns were about the same. Thus I found the *reported* death-rate from infectious disease in American cities to be about fifty per cent. But how many diseases are now recognized to be of bacterial origin without being entered as infectious in the official records; for instance, gonorrhœa, syphilis, the different forms of malaria, anthrax, pneumonia, endocarditis, pleurisy, peritonitis, rhinoscleroma, xerosis, influenza, yellow atrophy of the liver, lepra, whooping-cough, a great number of skin diseases, and a host of others. The statistics in the *Boston Journal* contain, besides what I have mentioned, a column of deaths from diarrhœal diseases as follows (omitting the decimals): New York, twenty-one per cent.; Brooklyn, nineteen per cent.; Boston, twenty per cent.; Baltimore, twenty per cent.; Cincinnati, twenty-seven per cent.; Charleston, thirty-six per cent., etc. The great majority of these deaths, if not all, may be considered as due to germ-disease. If we add these twenty per cent. to the above, and reckon the deaths from pneumonia and the other diseases which I mentioned before, with only ten per cent. of fatal termination, we obtain a death-rate from bacterial diseases of over eighty per cent. It is to be noted that these statistics were compiled when there was no epidemic prevailing. And, gentlemen, this is not all. I have not said a word of the numerous deaths of surgical disease, which, if we except fatal hemorrhage and coarse injury to important organs, may all be attributed to the deleterious influences of bacteria. Add these to the

above eighty per cent. with any quota you choose and you will see that, unless I have made a gross mistake, the professor of Berlin, in attributing the vast majority of all diseases to bacterial influences, has said the truth.

It is the knowledge and control of these influences that has, in the last ten years, so surprisingly reduced the death-rate from external diseases, and raised surgery to the proud position it now occupies.

In the advance of medical science surgery takes the lead at the present day, just as, according to Professor v. Bergmann, ophthalmology did at the time of v. Gräfe. It will, therefore, not be without interest and value to inquire what principle has infused such vital power into modern surgery, and whether this principle is likely to advance the other branches of medicine in a like manner. The key-note of modern surgery is expressed by the word antiseptis, which is the application of one branch only of bacteriology. Its scientific foundation is expressed by the words, Fermentation, Putrefaction, and Suppuration, which, in compliance with our president's kind invitation, I have chosen for the subject of my discourse this evening. In presenting this subject to you I shall follow its historical development, passing rapidly over the acquisition of our knowledge on fermentation and putrefaction, but dwelling on the important question of suppuration, in the solution of which a thousand hands are now busily at work with tools so refined, methods of investigation so accurate, and minds so scientifically trained as previous generations had not at their command.

Fermentation.—The scientific study of fermentation began with the investigations of Lavoisier, Fabroni, Thenard, and others, about a hundred years ago. These investigators thought it was a simple chemical decomposition.¹

Appert preserved animal and vegetable substances by

¹ For details of the following historic review, I refer to Mr. W. W. Cheyne's excellent book, *Antiseptic Surgery*.

putting them in bottles, well corked, and exposed to a temperature of boiling water.

Gay Lussac (1810) found that in substances preserved in such bottles for years, fermentation was started by letting in a small quantity of oxygen, but then it went on without it, and produced an inordinate quantity of carbonic acid. He declared that oxygen was necessary to initiate fermentation, but not to keep it up. For him fermentation remained a mysterious phenomenon, setting in tardily and proceeding slowly, quite different from other chemical processes.

In 1835 Cagniard-Latour discovered the yeast-plant, and added to this curious *fact* of observation an *idea*, namely, that the yeast causes sucre to ferment by some action of its vegetation and of its life.¹ He found also that the yeast-globules multiplied by budding, whence the name "budding fungi, sprouting fungi," *Sprosspilze* in German. A year later Turpin described the yeast of beer as a vegetable microscopic organism, which he termed *Torula cerevisiæ*.²

In 1836 Franz Schulze³ proved that fermentable and putrescible substances did not decompose if, after they had been boiled, the access of atmospheric air was prevented, for instance, by a layer of oil, or if the air, before it reached the substance, had passed through sulphuric acid or some other liquid which retained or destroyed the germs contained in the air. I show you the apparatus as simplified by Pouchet. Urine that was boiled two months ago in a glass retort, which, when cooling, received atmospheric air through a system of Liebig's bulbs partially filled with strong sulphuric acid, is now as clear as when freshly voided.

In 1837 the subject was taken in hand by Schwann, and "to him rather than to Cagniard-Latour must be

¹ E. Duclaux : *Le Microbe et la Maladie*, p. 6. Paris, 1886.

² Trouessart; *Microbes, Ferments, and Moulds*, 1885. Translated in Appleton's International Scientific Series, 1886. \$1.50, with 107 illustrations. A very entertaining introduction to bacteriology.

³ Gilbert's *Annalen der Chemie u. Physik*, 1836. vol. xxxix., p. 487.

given the credit of the first real proof of the view that the yeast-cells were the real cause of fermentation.”¹ Schwann’s apparatus, which I place before you, and with which I have repeated his experiments, consists of a glass retort from which glass tubes lead on the one side into a beaker containing mercury, corrosive sublimate, and olive-oil, on the other form a coil and end in a fine point. In the retort meat is boiled until the life of all substances contained in the apparatus, including germs adherent to its walls, is destroyed. The tapering end of the free tube, through which, during the cooling of the retort, the air entered and was sterilized by heating the coil, is hermetically sealed. [The apparatus and its working are demonstrated.] The meat did not putrefy. Schwann made similar experiments on alcoholic fermentation, thus *proving that the air contains some substance which is destructible by heat, and causes putrefaction and fermentation. The gases of the air, being unalterable by heat, cannot be the cause of these processes.*

Helmholtz, after repeating and confirming Schwann’s experiments,² made a very conclusive experiment, demonstrating that oxygen was not the cause of putrefaction. A meat infusion was boiled in a vessel, into which two platinum electrodes were fixed. After a time long enough to show that no fermentation would take place, an electric current, decomposing a part of the water, was sent through the liquid. The liquid remained pure.

In 1854³ Schröder and von Dusch examined whether *filtration of the air* would be sufficient to prevent fermentation of boiled liquids. Their apparatus [which was demonstrated] consisted in a retort in which a fermentescible substance was boiled. From its neck a tube connected on one side with a jar having a stop-cock near its bottom, on the other side with a larger tube, which was filled with cotton that had been so heated as to destroy in it all animal and vegetable life. When the boiling had

¹ Cheyne, *Antis. Surg.* p. 6.

³ *Annalen der Chem. und Physik.*

² Müller’s *Arch.*, 1843.

been prolonged long enough to purify the inner walls of the whole apparatus the stop-cock was opened, and as the water was slowly running out fresh air entered through the open tube on the other side, passing through the cotton filter before it reached the retort. The substances in the latter did neither ferment nor putrefy.

Another series of experiments (by Pasteur, Lister, Tyndall, and others) furnishes proof that the air can be purified by letting the particles suspended in it *settle by gravitation*. These investigators employed glass vessels, with tubes having one or several angular bends. I show you three such vessels in which grape-juice, meat-infusion, and milk were boiled four weeks ago. During and after the slow cooling the outside atmospheric air communicated with the air inside the flasks by the bent tubes, and you see that the contents in the three flasks are clear and sweet, whereas specimens taken from the same boiled liquids, on the same day, and left standing in open test-tubes, are decomposed.

The microscope has shown that all fermenting substances contain yeast-plants, and experiments, in various ways, have demonstrated that no fermentation takes place as long as the fermentescible substance is kept free from living yeast-cells. The presence of microbes thus being an essential factor in fermentation, the definition of fermentation ought to express it. We may therefore define fermentation as the *decomposition of carbo-hydrates into simpler compounds by the agency of living microbes*.

Putrefaction is a similar process. The decomposable substance contains nitrogen and sulphur besides carbon, hydrogen, and oxygen. The action of living bacteria is as essential in putrefaction as in fermentation. The species or varieties of these putrefactive micro-organisms are quite numerous. They do not belong to the class of budding fungi, but are fission fungi, either cocci or bacilli. Putrefaction apart from cold, heat, and exsiccation, can be prevented by the same methods which we have considered before. Germs in the putrescible sub-

stance, and the vessel which contains it, must be destroyed by heat or chemical substances, and the air, or any object coming in contact with it, must be germ free. The air can be purified (sterilized) by the same four ways which we have discussed in preventing fermentation: 1, By washing it (Fr. Schulze); 2, by heating (Schwann); 3, by filtration (Schröder and von Dusch), and 4, by rest and gravitation, the organic as well as the inorganic particles falling to the floor.

The products of putrefaction are CO_2 , H, H_2S , butyric and other fatty acids, ammonia, tyrosin, etc. If there is sufficient access of air (O), there is but little foul smell, H_2O , CO_2 , and NH_3 are formed, and the process is called mouldering (*Verwesung*), whereas by insufficient access of air foul-smelling products, H_2S and fatty acids are formed, besides the others, and the process is called putrefaction (*Fäulniss*).

Suppuration.—Is suppuration identical with, or the consequence of, putrefaction? Are the surgeons correct when they say, avoid putrefaction and there will be no suppuration, operate aseptically, treat a wound antiseptically, etc. As long as I believed in the mechanical or biological origin of suppuration, in contradistinction to its specific, *i.e.*, bacterial or parasitic origin, I thought the confusion of these different terms was wrong. But since it was demonstrated that the same species of bacteria produce suppuration as well as putrefaction, those surgeons were justified who, from practical experience, used these terms promiscuously, and more or less interchangeably. The pyogenic fungi will, for instance, curdle and decompose milk, and from putrefying substances bacteria are obtained that have a strong pyogenic action.

Moreover, the suppurating substances are of the same nature as the putrescible; chiefly albuminoids, containing C, H, O, N, and S. The difference only is that suppuration has relation to living, putrefaction to dead substances or tissues. Both are split in simpler and analo-

gous compounds. Yet there is one point not completely settled; is the intervention of bacteria as strictly a necessity—*a cenditio sine qua non*—in suppuration as it is in putrefaction? Many surgeons, judging from the results of antiseptic precautions, have keenly maintained this principle to be, at least, practically true. Scientific research has more and more verified it, and quite recently a few investigators have, on the strength of rigorous experiments, declared that there is no suppuration whatever without the action of living bacteria. Your humble servant, who has followed this question with a keen and unswerving attention, has, until lately, not been so radical. I thought, as the majority of physicians, that bacteria might be a cause of suppuration, but not the only one. Brought up in the ideas of cellular pathology, it seemed natural to me that irritants of different nature might cause white blood-corpuscles to pass through the walls of the vessels and accumulate, together with the movable lymphoid cells, at certain places of the tissue toward which the currents of the juices drove them. A celebrated experiment of Recklinghausen shows a proliferation of the movable contractile corneal corpuscles, after a frog or cat's cornea has been cauterized in the centre and placed, under appropriate conditions, on the object-table of a microscope for from one to three days. Another similar experiment appeared to me convincing of the possibility of a traumatic origin of suppuration. When a fresh frog's cornea is placed on the heated object-table of a microscope, and watched for an hour or two, we notice that the movable corpuscles emigrate from the tissue to the cut edge. There they cluster and apparently form a streak of pus.

The question of the formation of pus seemed to me of such fundamental importance that I took it up experimentally, and studied it under the following heads:

1. Does traumatism of any kind produce suppuration?
2. Do foreign bodies occasion the formation of pus?

3. Are there any kinds of chemical agents that cause suppuration?

1. On the first question I made a series of experiments in Berlin last winter, and published them in the "Archives of Ophthalmology."¹ I performed all the operations that are practised on the eye, on the one side of a rabbit, with sterilized instruments, in an aseptic way; on the other side the wound was contaminated with an emulsion of a pure culture of some pyogenic fungus. All the former healed by first intention, the latter suppurated with the regularity of a chemical experiment. Since that time I have repeated these experiments, with the same result, and for the sake of illustration I pass round a rabbit, operated on two weeks ago by students, during one of my lectures at the University Medical College. You see that the right eye shows a smooth scar with a perfectly clear eye, whereas the left, where an impure extraction of cataract had been made, shows a deformed eye, a large yellow staphyloma, after suppuration of the wound. Experimenting in this way with pure and contaminated material before the students, and letting them operate on animals in the same way, makes the instruction unusually impressive, convincing, and suggestive. The most persuasive didactic lecture on suppuration falls flat before an audience that has once witnessed two operations performed on the same animal, in the same way, by the same hands, with the only difference that the point of the knife during the second operation was dipped into an emulsion of *staphylococcus pyogenes albus*. The next day no irritation in the first wound, but the hideous picture of a phlegmonous inflammation in the other. The coarsest operation, the rudest treatment of a wound will not be followed by suppuration if only the pyogenic germs are excluded. In extractions of cataract (in rabbits, of course) I have purposely bruised and lacerated the iris, evacuated almost all the vitreous, then stirred

¹ Vol. xv., p. 24, March, 1886.

up the rest with a platinum needle that had previously been brought to a glow, and finally scratched with the same needle the ciliary processes in every direction, yet no suppuration ensued; whereas the smoothest and most cautious operations were invariably followed by suppuration when the wound was contaminated in some way by pyogenic fungi, I say pyogenic, not other fungi. Surgeons have long come to this conclusion; yet the experimental test is more convincing than long series of operations, because it furnishes direct evidence by making in the primary and verifying experiments all things equal, except the presence or absence of a certain kind of micro-organism. These micro-organisms are now obtained unadulterated with other material, *i.e.*, in pure cultivations. Gradually we become as well acquainted with their morphological and biological properties as we are with the chemical and physical properties of organic or inorganic bodies. If the addition of a certain microbe determines the result of one of two otherwise equal experiments invariably and unambiguously in a certain direction, if the microbe can be obtained again from the one animal, but not from the other, and if, in new experiments, it always brings about the same results, then we may fairly say that the microbe is the cause of the phenomenon.

If in these cases microbes cause suppuration, are we allowed to conclude that every suppuration is caused by microbes? Not from this fact alone. One of the fundamental observations that led to the introduction of antiseptic surgery was the fact that simple fractures heal without suppuration. But there is an occasional exception to this rule, and a law of nature is never established as long as the exceptions are not explained. In the exceptional cases of suppuration after a simple fracture, a focus of suppuration somewhere else in the body has either been discovered, or its presence can be assumed with certainty. The experimental proof of this fact has been furnished of late by Becker and F. Krause, who observed

that simple fractures in healthy animals regularly healed by first intention, but just as regularly suppurated when pyogenic microbes were injected into a vein of the ear. The same observation holds good with extravasated blood, hydrocele liquid, and other sequestered bodies when kept free from germs in a healthy animal. The experiments of Orth and Wyssokowitsch on ulcerated endocarditis furnish argument in the same line, and the famous operation of bistournage by Chauveau has the entire force of a faultless experiment. This galaxy of facts, which might be increased indefinitely, furnishes indisputable evidence that *mere traumatism, of whatever kind, never causes suppuration.*

2. The second question, *Do foreign bodies, as such, cause suppuration*, may be answered in brief, for Theo. Leber and others have experimentally studied and brought it to a certain final solution. Leber states that indifferent, non-oxidizable foreign bodies, aseptically introduced into the tissues or cavities of the human body, cause no inflammation, in particular no suppuration.¹ I have introduced a number of foreign bodies—for instance, pieces of a hair-pin—aseptically, into the anterior chamber. The hair-pin was old, rusty, and dirty. It was not cleansed, but before its introduction it was brought to a glow. A small piece of the periphery of the cornea was cauterized with a glowing strabismus hook, pierced with a sterilized small knife, the pin was introduced with an aseptic little forceps, pushed more deeply into the anterior chamber, and the wound-canal again sealed with the glowing hook. The foreign bodies caused no suppuration, they lay either free on the iris, or were surrounded by a delicate, apparently fibrous, exudation. In one rabbit (which I show you here), the foreign body in the right eye has been well borne, and lies in the anterior chamber, one end encapsuled, the other free, whereas the most violent phlegmon broke out in the

¹ Trans. Seventh International Medical Congress, 1881, vol. iii., pp. 15-19.

other eye in the first twenty-four hours, and destroyed the globe completely. A similar piece of the same hair-pin had been brought to a glow and introduced in the same way, with the only difference that before the introduction it had been dipped into an emulsion of staphylococcus pyogenes albus. By these and similar experiments previous views, even if entertained by scientists of the greatest merit, are refuted. Among the supporters of the possibility of suppuration by the action of foreign bodies I may mention Pasteur, who, in 1878, claimed to have discovered the *microbe du pus*, derived from hydrant water. Nevertheless he pretended, on the strength of his experiments, that suppuration could be caused by foreign bodies introduced under the skin aseptically. J. Straus found that solid bodies aseptically introduced under the skin, produced no suppuration. Of his excellent method I shall speak presently.

3. I come to the last and most critical question of my subject, *Do chemical agents cause suppuration without the intervention of microbes?* This question has been answered positively by all but a few very recent investigators. Baumgarten, Theo. Leber, Uskoff, Orthmann, Councilman, Rosenbach, Passet, and others, assert having convinced themselves that suppuration is caused by certain chemical agents, for instance mercury, oil of cantharides, petroleum, turpentine, and, above all, croton-oil, even if aseptically introduced. Four recent observers, however, contest this assertion on the strength of new and more rigorous experiments. The leading investigator among these four is J. Straus, who for the first time used a perfect aseptic method.¹ A sterilized glass tube, tapering in a point on one side, closed with a sterilized cotton plug on the other, was filled with sterilized croton-oil, and the point sealed up. He sterilized the skin of the animal by singeing it with Paquelin's cautery, stabbed

¹ Comptes Rendus hebdomadaires des Séances de la Société de Biologie, December 15, 1883, p. 651.

it with a sterilized knife, introduced the thin end of the tube, broke off its point, blew through the cotton plug the oil out into the subcutaneous tissue, withdrew the tube, and sealed the wound-canal by burning its orifice with the cautery. Among 18 injections of turpentine 13 did not produce suppuration; of 5 injections of croton-oil 1 suppurated; of 2 injections of mercury none suppurated. When suppuration ensued he found cocci in the pus.

E. Scheuerlen¹ repeated the experiments of Councilman-Cohnheim,² with greater antiseptic precautions, in the laboratory of the surgical clinic (Bergmann's) of Berlin, under the auspices of Dr. Gaffky and Dr. Fehleisen. Small glass capsules, the ordinary vaccine tubes, were sterilized in a Koch steam sterilizer for half an hour, then, by means of a canula needle and a small piston, thrust under the skin of rabbits. Before the operation the skin in the region of the operation had been carefully shorn, and disinfected with a 1 to 1,000 corrosive sublimate solution. After the introduction, the little tube lay in the subcutaneous tissue about ten millimetres distant from the puncture of the skin. The region of the puncture was covered with a thick layer of iodoform collodium. He used about a dozen irritating substances, among others turpentine and croton-oil. A week or ten days after the introduction of the little tubes, when they lay free from irritation under the skin, and the small wound was perfectly healed, they were broken. A hard swelling occurred around them, but suppuration only in one of his thirty-two experiments (croton-oil), in which a puriform exudation extended from the skin all along the stab-wound. In this case the sterilization and healing had been imperfect, and bacteria, which were found in the purulent exudation, must have penetrated into the wound. In no other case were bacteria found in the infiltrated tissue around the broken capsule.

¹ Langenbeck's Arch., 1885, vol. xxxii., p. 500.

² Virchow's Arch., 1883, vol. xcii., p. 217.

In 1885 a very instructive series of experiments was made by George Klemperer,¹ in Professor Leyden's laboratory at Berlin. Klemperer made injections of different substances, chiefly turpentine and croton-oil. He used Koch's syringe, sterilized in boiling water, and disinfected the skin of the animals by cauterizing it with glowing iron according to Straus. He also made a number of experiments with the glass capsules of Cohnheim and Councilman. Only in a few experiments, in which the precautions had been insufficient, he obtained pus, recognizable as such macroscopically and microscopically. Bacteria were found in it with the microscope and by cultivations. In all other cases he found sero-fibrinous exudation with coagulation-necrosis (Weigert), no bacteria by both microscopic and cultivation tests.

The last author I have to mention is Dr. J. A. Ruys. He made a series of experiments in the Pathological Laboratory of the University of Utrecht, and published them, November, 1885, in the *Deutsche Medicin. Wochenschrift*.² He chose the anterior chamber as the best place of experimentation, because the occurring changes could be directly watched from day to day. He injected one or two drops of turpentine or of a mixture of equal parts of croton and olive oils, or petroleum. Only in one of his twenty-one cases he obtained suppuration, in all others he noticed in the anterior chamber a fibrinous exudation, which in a shorter or longer time gradually was absorbed. When the animals were killed and the fibrinous exudation in the anterior chamber was examined, fibrine and leucocytes were found, but no bacteria. Cultivations from the exudation remained sterile. As verifying experiments Ruys introduced into the anterior chamber silk threads impregnated with the oil and an emulsion of staphylococcus pyogenes. Suppuration ensued.

The last-named four authors draw from their experi-

¹ Zeitsch. f. klin. Med., vol. x., Nos. 1 and 2.

² Vol. xi., p. 825.

ments the conclusion that *bacteria are the cause of every suppuration.*

This unconditional opinion, gentlemen, is not generally accepted. Even in Berlin where it has the strongest supporters, I found, last winter, the most competent bacteriologists unwilling to adopt it without reserve. It may be so, they said, but thus far it is not demonstrated beyond a doubt. I thought it therefore particularly desirable to subject the third question : *Do chemical agents cause suppuration,* to a further experimental inquiry. In my experiments (they are not yet concluded) I used turpentine and croton-oil, because these two substances have proved the most powerful to initiate or favor suppuration. The action of pure turpentine being less pronounced than that of croton-oil, the majority of my experiments have been made with the latter. Yet some experiments with the former may deserve mention.

Three weeks ago I injected a drop or two of pure sterilized turpentine, with a sterilized Koch's syringe, into the anterior chamber of a rabbit which I show you here. The next day white patches developed in the upper parts of both anterior chambers, no sediment in the lower parts. The patches grew larger and more intense, somewhat resembling corneal pustules. On the fifth day the upper part of the left cornea had become white, and there were some white patches also in the lower part. This condition looking like suppuration, I enucleated the eye, and found in the anterior chamber some flaky deposits on the posterior face of the cornea, of which I made microscopic preparations and four cultivations. The microscopic specimens showed fibrine and lymphoid corpuscles, but no microbes whatever. One of the specimens is under a microscope for your kind inspection. The four culture-tubes which I pass round have all remained sterile. The exudation, therefore, was not purulent, but fibrino-leucocytic. The three nodules in the anterior chamber of the other eye remained stationary for a few days and then began gradually and slowly to

disappear. You see now that they have left a trace, but the eye is in good condition.

Turpentine, injected aseptically and in small quantities under the skin, produced some hard swelling, which in the second week began to disappear.

Sterilized turpentine, sixty-six centigrammes, injected into the abdominal cavity of a rabbit, produced no effect either objectively or subjectively. When the animal was killed, at the end of two weeks, no abnormality was found in the abdominal cavity.

Turpentine injected in both anterior chambers of a rabbit produced the same congestion of the iris and the patchy opacity in the upper parts of the anterior chambers as before described. It gradually was absorbed, and the eyes recovered.

The results of the experiments with turpentine were clear and easily obtained; not so those with croton-oil, the *crux experimentatorum*. At first I used croton-oil pure, sterilized, and injected it into the anterior chamber according to Ruys' method, singeing the place of puncture before and after the injection. A portion of the oil flowed out again, producing purulent discharge and diphtheroid deposits of the conjunctiva, and so much blistering of the skin that the surroundings of the eye were denuded to a considerable extent, the cornea ulcerated and sloughed, and the eye atrophied. [Rabbit demonstrated.]

Being as careful as I could, I did not succeed in obtaining clean results with injections of croton-oil into the anterior chamber. Through the cornea there always was more or less puriform discharge from the conjunctiva, and though in the first three or four days the drop of oil was clearly seen at the upper border of the anterior chamber, the cornea became hazy, ulcerous, sloughed, and the majority of eyes were lost. Those which I removed before they burst showed no pus in the anterior chamber, but a flaky substance which neither on cultivation nor under the microscope discovered any microbes.

Pure croton-oil, injected under the skin, aseptically,

the skin disinfected with the actual cautery before and after the introduction of the point of the syringe, produced a hard swelling, which, being incised, showed no pus, and under the microscope and in cultivations no microbes. In one case such a hard lump sloughed out with sharp, deep edges as if punched out. The wound healed rapidly without suppuration. Klemperer, whose experiments consisted almost exclusively in subcutaneous injections of different *acria*, has studied this mortification of tissue—Weigert's coagulation necrosis—particularly, and describes it well (*l. c.*).

As these experiments lack the demonstrative directness of the injections into the anterior chamber, I endeavored to modify Ruys' method, so as to obtain clean results. I injected a sterilized mixture of one part of pure croton-oil and two parts of olive-oil into the anterior chamber of the right eyes of four rabbits, thrusting the thoroughly sterilized syringe through the sclerotic, lens, and pupil into the anterior chamber. As soon as the opening of the point presented in the pupil I pressed upon the rubber ball, and one or two drops escaped and mounted to the top of the anterior chamber, without disturbing the iris or producing any apparent change in the size and configuration of the chamber. The left eyes of the same rabbits were experimented on in the same way; the croton-oil, however, was mixed with a very small quantity of a pure culture of *staphylococcus aureus* on agar-agar. After the syringe was withdrawn the point of puncture in the sclerotic was sealed up with a glowing strabismus-hook. The next day the right eyes showed moderate reaction, the drop of oil was distinctly visible in the upper part of the anterior chamber; pupil, iris, and cornea clear. The left eyes discharged pus from the conjunctiva, were swollen, the irides very red, the contents of the anterior chamber muddy. On the third day two of these rabbits died. The right eyes had only a few flakes, no pus in the anterior chamber; their vitreous was clear. The left eyes

showed a hemorrhagic exudation, with coherent flakes, and soft, purulent patches in the anterior chamber, and purulent patches in the vitreous. Cultivation and microscopic specimens showed no, or only a few, microbes in the right eyes, but multitudes of microbes in the left.

On the fourth day another rabbit died. Result of the examination the same: Fibrino-leucocytic exudation in the right eye, hemorrhagic, and purulent exudation, with multitudes of microbes, in the left.

The fourth rabbit of this series showed no particular reaction in the right eye. The cornea was hazy, iris and pupil, however, visible. Left eye enlarged, a yellow deposit in lower third of anterior chamber. Animal looked sick, but was not moribund. Killed on the seventh day. In right no pus; some exudation in iris angle, vitreous turbid. Left eye: anterior chamber and vitreous cloudy, containing puriform patches. Dry cover-specimens and cultivations were made from both eyes, and many organs, with the following results: The microscopic specimens showed a few unmistakable cocci in the right eye, multitudes in the left.

Cultivations after seven days: Right anterior chamber one small colony, right vitreous four small colonies. Left anterior chamber and vitreous, luxuriant growths, liquefying gelatine on the third day. Blood from heart, six isolated colonies; blood from kidney, four well-developed colonies. Brain, none.

I have still to add that in this group of rabbits I injected aseptically small quantities of sterilized croton-oil under the skin of the back of the right side, and the same, contaminated with staphylococcus aureus, under the skin of the back of the left side. In neither was there any remarkable reaction. Yet from the left sides tolerably well-developed growths were obtained. In the three before-mentioned rabbits cultivations were made from both eyes. Anterior chamber and vitreous showed abundant growths in the left (infected) eyes, very scant growths from the right.

How shall we interpret these results? Suppuration with luxuriant growths of cocci in the infected organs, some flaky fibrino-leucocytic exudation in the eyes into which croton-olive oil sterilized, and with, it seems, sufficient antiseptic precautions, had been injected, yet these eyes contained some cocci. The answer is given by the more extensive examination of the body of the fourth rabbit. Suppuration with multitudes of cocci was found in the infected eye; no suppuration, but some cocci, were found in the blood, the kidneys, and the other eye. From the focus of suppuration the cocci had passed into the blood and were deposited in the kidneys, the chief place of their elimination, and in the other eye, which by the injection of croton-oil was irritated and in a fit condition for their development.

To remove this uncertainty I made another series of experiments five days ago. Sterilized croton-olive oil was injected into the right eyes of three rabbits, and an emulsion of the same and staphylococcus albus into the left eyes of three other rabbits. The needle of Koch's syringe was introduced through the ciliary body, and advanced close behind the iris until it presented in the pupil. After the withdrawal of the syringe the puncture in the sclerotic was sealed with the actual cautery. The experiments succeeded very well and were remarkably clean. The results were striking; the infected eyes suppurated freely, the others showed only some whitish streaks in the upper parts of the cornea, descending in two rabbits along the posterior surface of the cornea. One of these eyes was enucleated yesterday. There was no pus in the anterior chamber, the vitreous was clear and the inner membranes were healthy. The streaks at the posterior face of the cornea presented themselves as whitish deposits. Under the microscope they consisted of networks and pencils of coagulated fibrine, and of epithelial cells of Descemet's membrane isolated and in clusters. Adherent to these cells and scattered in the specimen were numerous oil-globules;

no trace of microbes. Cultivations taken from the striated deposit, kept in a warm room these twenty-four hours, show as yet no growth.

Mr. President and Gentlemen, I have reported substantially on all the experiments I have made. I shall continue them, principally according to the last-named method, which promises to give unambiguous results. As far as these experiments go, and in consideration of like results obtained by some recent investigators, they furnish, it seems to me, sufficient evidence of the truth of the proposition, that *suppuration in every case depends on the action of microbes*. If, on the one hand, traumatism of any kind, if foreign bodies, if the most irritant chemical agents, if anything you may imagine is not of itself capable of producing suppuration; if, on the other hand, the addition of pyogenic microbes to any irritating substance, or wound, or any lesion whatsoever, produces, under proper conditions, suppuration without fail, we are certainly justified in ascribing to pyogenic germs the causative action in the formation of pus.

In conclusion, gentlemen, two words. What is pus? "An albuminous, non-coagulable fluid containing multitudes of leucocytes." What is suppuration? "The splitting of living nitrogenous tissue into simpler compounds through the influence of certain bacteria." In this way the parallelism of the three processes—fermentation, putrefaction, and suppuration—is established.